CLN1 disease

CLN1 disease is an inherited disorder that primarily affects the nervous system. Individuals with this condition have normal development in infancy, but typically by 18 months they begin to lose previously acquired skills (developmental regression). In affected children, brain cells die over time, leading to an overall loss of brain tissue (brain atrophy) and an unusually small head (microcephaly). Children with CLN1 disease have decreased muscle tone (hypotonia), intellectual and motor disability, and rarely are able to speak or walk. Individuals with this condition often have muscle twitches (myoclonus), recurrent seizures (epilepsy), and vision loss. Children with CLN1 disease usually do not survive past adolescence.

Some people with this condition do not develop symptoms until later in childhood or in adulthood. As with younger affected children, older individuals develop a decline in intellectual function, myoclonus, epilepsy, and vision loss. Adults with CLN1 disease may also have movement disorders, including impaired muscle coordination (ataxia) or a pattern of movement abnormalities known as parkinsonism.

CLN1 disease is one of a group of disorders known as neuronal ceroid lipofuscinoses (NCLs), which may also be collectively referred to as Batten disease. All these disorders affect the nervous system and typically cause worsening problems with vision, movement, and thinking ability. The different NCLs are distinguished by their genetic cause. Each disease type is given the designation "CLN," meaning ceroid lipofuscinosis, neuronal, and then a number to indicate its subtype.

Frequency

The incidence of CLN1 disease is unknown; more than 200 cases have been described in the scientific literature. Collectively, all forms of NCL affect an estimated 1 in 100,000 individuals worldwide. NCLs are more common in Finland, where approximately 1 in 12,500 individuals are affected.

Genetic Changes

Mutations in the *PPT1* gene cause CLN1 disease. The *PPT1* gene provides instructions for making an enzyme called palmitoyl-protein thioesterase 1. This enzyme is active in cell compartments called lysosomes, which digest and recycle different types of molecules. Palmitoyl-protein thioesterase 1 removes fats called long-chain fatty acids from certain proteins, which helps to break down the proteins. Palmitoyl-protein thioesterase 1 is also thought to be involved in a variety of other cell functions.

PPT1 gene mutations that cause CLN1 disease decrease or eliminate the production or function of palmitoyl-protein thioesterase 1. A reduction of functional enzyme impairs

the removal of fatty acids from certain proteins. These partially broken down fats and proteins accumulate in lysosomes. While accumulations of these substances occurs in cells throughout the body, nerve cells appear to be particularly vulnerable to damage caused by the abnormal cell materials. Early and widespread loss of nerve cells in CLN1 disease leads to severe signs and symptoms and death in childhood.

In the later-onset cases of CLN1 disease, *PPT1* gene mutations result in the production of a palmitoyl-protein thioesterase 1 enzyme that has a reduced level of normal function; however, protein function in these individuals is higher than in those who have the condition beginning in early childhood. As a result, long-chain fatty acids are removed from some proteins, allowing for a small amount of proteins to be broken down. Since it takes longer for these substances to accumulate in lysosomes and cause nerve cell death, the signs and symptoms of CLN1 disease in these individuals occur later in life.

Inheritance Pattern

This condition is inherited in an autosomal recessive pattern, which means both copies of the gene in each cell have mutations. The parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but they typically do not show signs and symptoms of the condition.

Other Names for This Condition

- CLN1
- infantile Batten disease
- infantile neuronal ceroid lipofuscinosis
- neuronal ceroid lipofuscinosis 1
- neuronal ceroid lipofuscinosis, infantile
- Santavuori-Haltia disease

Diagnosis & Management

Genetic Testing

- Genetic Testing Registry: Ceroid lipofuscinosis neuronal 1
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C1850451/
- Genetic Testing Registry: Infantile neuronal ceroid lipofuscinosis
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C0268281/

Other Diagnosis and Management Resources

- GeneReview: Neuronal Ceroid-Lipofuscinoses
  https://www.ncbi.nlm.nih.gov/books/NBK1428

General Information from MedlinePlus

- Diagnostic Tests
  https://medlineplus.gov/diagnostictests.html
- Drug Therapy
  https://medlineplus.gov/drugtherapy.html
- Genetic Counseling
  https://medlineplus.gov/geneticcounseling.html
- Palliative Care
  https://medlineplus.gov/palliativecare.html
- Surgery and Rehabilitation
  https://medlineplus.gov/surgeryandrehabilitation.html

Additional Information & Resources

MedlinePlus

- Encyclopedia: Neuronal Ceroid Lipofuscinoses (NCLS)
  https://medlineplus.gov/ency/article/001613.htm
- Health Topic: Degenerative Nerve Diseases
  https://medlineplus.gov/degenerativenervediseases.html
- Health Topic: Vision Impairment and Blindness
  https://medlineplus.gov/visionimpairmentandblindness.html

Genetic and Rare Diseases Information Center

- Ceroid lipofuscinosis neuronal 1
  https://rarediseases.info.nih.gov/diseases/1219/ceroid-lipofuscinosis-neuronal-1

Additional NIH Resources

- National Institute of Neurological Disorders and Stroke: Batten Disease Fact Sheet
  https://www.ninds.nih.gov/Disorders/All-Disorders/Batten-Disease-Information-Page
- National Institute of Neurological Disorders and Stroke: Myoclonus Information Page
  https://www.ninds.nih.gov/Disorders/All-Disorders/Myoclonus-Information-Page

Educational Resources

- Baylor College of Medicine: Myoclonus
  https://www.bcm.edu/healthcare/care-centers/parkinsons/conditions/myoclonus
- CLIMB Information Sheet: Batten Disease--Infantile Form
  http://www.climb.org.uk/IMD/Bravo/BattenDisease-InfantileForm.pdf

- Disease InfoSearch: Ceroid Lipofuscinosis Neuronal 1
  http://www.diseaseinfosearch.org/Ceroid+Lipofuscinosis+Neuronal+1/1250
- Disease InfoSearch: Neuronal Ceroid Lipofuscinosis
  http://www.diseaseinfosearch.org/Neuronal+Ceroid+Lipofuscinosis/5192
- Orphanet: Infantile neuronal ceroid lipofuscinosis
  http://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=79263
- The University of Arizona
  http://disorders.eyes.arizona.edu/disorders/neuronal-ceroid-lipofuscinoses
- University College London: What is Batten Disease?
  http://www.ucl.ac.uk/ncl/batten.shtml

Patient Support and Advocacy Resources

- American Association on Intellectual and Developmental Disabilities (AAIDD)
  http://aaidd.org/
- Batten Disease Family Association
  http://www.bdfa-uk.org.uk/cln1-disease-infantile-onset-and-others/
- Batten Disease Support & Research Association
  http://bdsra.org/
- Beyond Batten Disease Foundation
  http://beyondbatten.org/
- CLIMB: Children Living with Inherited Metabolic Diseases
  http://www.climb.org.uk/

GeneReviews

- Neuronal Ceroid-Lipofuscinoses
  https://www.ncbi.nlm.nih.gov/books/NBK1428

ClinicalTrials.gov

- ClinicalTrials.gov
  https://clinicaltrials.gov/ct2/results?cond=%22infantile+neuronal+ceroid+lipofuscinosis%22+OR+%22Santavuori-Haltia+disease%22+OR+%22Neuronal+Ceroid-Lipofuscinoses%22

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28PPT1%5BTIAB%5D%29+OR+%28cln1%5BTIAB%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1800+days%22%5Bdp%5D

OMIM

- CEROID LIPOFUSCINOSIS, NEURONAL, 1
  http://omim.org/entry/256730

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